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Original Article

DEVELOPMENT AND *IN-VITRO* EVALUATION OF QUANTUM DOTS AS A CARRIER FOR DELIVERY OF 5-FLUOROURACIL

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ABSTRACT

Objective: The present study was aimed to develop and evaluate quantum dots (QDs) as a carrier for delivery of 5-fluorouracil (5-FU).

Methods: This research work includes a synthesis, characterization and *in vitro* study of 5-fluorouracil (5-FU) QDs. Zinc oxide QDs were synthesized, and the drug was loaded on them. These QDs were further coated with Eudragit E PO to achieve drug release only at the acidic pH range as well as to overcome release of drug in the formulation vehicle itself.

Results: For 5-FU QDs optimized batch, yield (74±0.001 %), drug loading (85.58±0.08 %) and drug content (95±0.015%) were observed. FTIR spectroscopy revealed no any incompatibility between drug, polymer and metal SEM images shown drug loaded QDs with rough surface and Eudragit E PO coated QDs with smooth surface. The DSC curve of 5-FU exhibits peak at 286 °C corresponding to its melting point and Eudragit E PO coated QDs exhibit peak at 272 °C. This shifting of the endotherm suggested possible interaction of 5-FU and Eudragit E PO coated QDs. The diffractogram of pure drug showed multi-crystalline nature. However pure Eudragit E PO showed amorphous nature. Optimized QDs showed the crystalline nature of the drug. Mean particle size of optimized formulation batch was 201.92 nm and zeta potential was found+1.85 mV.

Conclusion: An Optimized batch of QDs has the potential to utilize in future for imaging of cancer cells and targeting delivery of 5-FU.

Keywords: Anti-cancer, 5-fluorouracil, Nanoparticles, Quantum dots, Targeted drug delivery.

INTRODUCTION

Quantum dots (QDs) are very tiny particles of about a nanometer in size. QDs consist of a semiconductor material with a diameter in the range of 2-10 nanometers. The color of Quantum dots depends on the size of the dot or particle. Quantum dots are a novel class of inorganic fluorophore, which are gaining widespread recognition due to their exceptional photophysical properties. Due to fluorescence property in them, when the light is emitted for them of a certain wavelength, it shows fluorescence light at targeted sites. This application of QDs is being used in imaging of the cells in the body, when these QDs are coated with the specific category of drug. These quantum dots possess a metal on which the drug is coated [1].

Quantum dots are emerging as a new class of fluorescent probes for biomolecular and cellular imaging. The nature of this technology makes it suitable for application such as *in vivo* imaging, including live cell and whole animal imaging, blood cancer assay, cancer detection and treatment [2].

A general QD comprises of three main parts. At the center of the structure, there is a single core having a diameter in nanometers, whose size and shape can be changed. Around this, the core is coated with the QD shell possessing the optical properties, as this shell contains the semiconductor metal. QD shell is then coated with the outer layer depending upon the application for which QDs are to be used [3].

The ability of quantum dots to glow fluorescence after reaching the target site can be used in a targeted drug delivery. As quantum dots coated with drug reaches the target site it causes the interaction between the surface charge of target cells and the charge of material. Due to such application of quantum dot it is used here as a carrier for an administration of the anticancer drug.

The small size of quantum dots allows them to go anywhere in the body, making them suitable for different biomedical applications like medical imaging, biosensors, etc. Photostability is one of the greatest advantages of QDs for in vivo applications since it allows images to be recorded over a longer period of time than available with the use of fluorescent dyes or proteins, due to resistance in photobleaching [4]. Many tumor types can be identified purely based on their image contrast [5]. Recent studies using quantum dots in neuroscience illustrate the potential of this technology. Antibody-functionalized quantum dots are used to track the lateral diffusion of glycine receptors in cultures of primary spinal cord neurons [6]. The drug used to coat QDs is 5-fluorouracil (5-FU), which is an anticancer drug that helps in treating most of the cancers of head, neck, breast, etc. Till date, solid lipid nanoparticles and polymeric nanoparticles had been prepared by using 5-fluorouracil. However, QDs of 5-fluorouracil have not been reported yet, so there was scope to formulate QDs.

MATERIALS AND METHODS

Materials

5-fluorouracil, an active pharmaceutical ingredient was obtained from Yarrow Chem Products, Mumbai, India. Eudragit E PO, used as polymer was obtained from Sava Pharmaceuticals, Pune, India. Methanol, nitric acid, chloroform, sodium hydroxide, potassium dihydrogen phosphate, disodium hydrogen phosphate were of analytical grade.

Methods

Calibration of 5-FU by using UV Spectrophotometer (Florey 2005)

First the wavelength of 5-fluorouracil by using methanol as a solvent was determined as depicted in (fig. 1). The calibration was carried out in methanol due to the higher solubility of the drug in it as shown in (fig. 2). Further, at obtained wavelength the calibration was carried out by preparing the samples of different concentrations (ppm). The samples were diluted if necessary. Later on, absorbance was measured, and it was seen that the range obeys the beer's and Lambert's law.

Preparation of zinc oxide (ZnO) quantum dots

According to this procedure, zinc chloride was dissolved in nitric acid (HNO_3) and to this mixture methanol was added and it was dried at a suitable temperature. Now this dried sample was dissolved in methanol. Sodium hydroxide, which was dissolved in methanol, was added in after

some time to zinc nitrate solution with vigorous stirring. The temperature was maintained for a specific period of time, and then the solution becomes translucent. After this time period, the quantum dots start to precipitate, and the solution becomes turbid. The heating and stirring of the sample were stopped and later on the precipitation of these nano particles was continued for an additional period of time. The precipitate was obtained, and the mother liquor was separated, and then the precipitate was washed with methanol as depicted in (table 1) [7].

Drug loading on ZnO quantum dots

Initially, QDs were dispersed in methanol. 5-FU was added to that mixture and 5-FU gets dissolved as it has solubility in methanol. Cold water was added slowly to QDs-drug mixture. The role of cold water is to coat 5-FU on the QDs. 5-FU came out and loaded up on the uncoated QDs. This drug loaded QDs were further dried in the oven at 70 °C as depicted in (table 2).

Polymer coating on drug loaded quantum dots

Firstly, Eudragit E PO polymer was dissolved in chloroform. Further, drug loaded QDs were weighed and then dispersed in the polymer solution. This mixture was kept in undisturbed condition for 15 min and then stirred. Later on, this mixture was filtered using Whatman filter paper. Finally, polymer-coated QDs were air dried for overnight as depicted in (table 3).

Preparation of batches of uncoated QDs

Table 1: Batches of uncoated QDs

Batch	Source of metal used	Quantity used	Quantity of nitric acid (0.1N) used	Quantity of methanol (99% v/v) used
B_1	$ZnCl_2$	0.0985 g	0.29 ml	5 ml
B_2	$ZnCl_2$	1 g	0.29 ml	5 ml
B_3	$ZnCl_2$	1 g	0.30 ml	5 ml
B_4	$ZnCl_2$	1.5 g	1 ml	10 ml
B_5	$ZnCl_2$	5 g	1 ml	7 ml

Preparation of batches of drug loaded QDs

Table 2: Batches of drug loaded QDs

Batch	QD: Drug	Solvent and volume of solvent used	Coating solvent
B_1	1: 0.5	Methanol-5 ml	Cold water-5 ml
B_2	1:1	Methanol-5 ml	Cold water-5 ml
B_3	1:1	Methanol-5 ml	Petroleum ether-5 ml
B_4	1:1	Methanol-5 ml	Acetone-5 ml
B_5	1:2	Methanol-5 ml	Cold water-5 ml

Preparation of batches of Eudragit E PO coated QDs

Table 3: Batches of Eudragit E PO coated QDs

Batch	Solvent and volume of solvent used	Quantity of QDs taken	Quantity of Eudragit E PO taken	Eudragit grade used
B_1	Chloroform-3 ml	2.5 mg	2%	Eudragit E 100
B_2	Chloroform-20 ml	10 mg	5%	Eudragit E 100
B_3	Chloroform-3 ml	2.5 mg	2%	Eudragit E PO
B_4	Chloroform-20 ml	10 mg	5%	Eudragit E PO

Eudragit E 100 and Eudragit E PO polymers were selected for coating over the drug loaded QDs. Due to unsatisfactory results of coating efficiency of Eudragit E 100, finally, Eudragit E PO was selected for loading, as it gave satisfactory results as compared to Eudragit E 100. Further, it was decided to incorporate Eudragit E PO coated QDs in chloroform as the Eudragit E PO is insoluble in it. So that, Eudragit E PO layer will not get dispersed into aqueous formulation vehicles. However, as the cancerous target tissues or cells have an acidic environment, Eudragit E PO is expected to get released in the pH range of 1-5 due to its solubility at this acidic pH range.

Characterization of 5-FU QDs

Differential scanning calorimetry (DSC)

DSC measurements were performed on a differential scanning calorimeter equipped with an intra-cooler (DSC Mettler STAR SW 9.20, Switzerland). The inert atmosphere was maintained by purging nitrogen gas at a flow rate of 50 ml/min. All accurately weighed samples (about 3-5 mg) were placed in a sealed aluminium pan, and the samples were heated under nitrogen gas flow (20 ml/min) at a scanning rate of 10 °C per min from 40 to 240º C. An empty aluminium pan was used as a reference. DSC analysis was performed for pure 5-fluorouracil as shown in (fig. 3) and Eudragit E PO coated QDs as shown in (fig. 4) [8].

X-ray diffraction studies (XRD)

X-ray diffraction studies provide information about the crystallinity of the sample, which is reflected by a characteristic fingerprint region in the diffraction pattern. Studies were carried out by using ORIGIN 8 Version 8E with a resolution of 0.001A °. Vacuum grease was applied over the glass slide to stick the sample. About 2 mg of sample was sprinkled over to form a layer. The samples were radiated using a Cu target tube and exposed to all lines (λ-1.54056). Scanning angles ranged from 5 ° to 40 ° of 2θ. The current used was 30 mA and voltage of 40 kV. X-ray diffraction studies of 5-FU as depicted in (fig. 5), Eudragit polymer as shown in (fig. 6) and Eudragit E PO coated QDs as shown in (fig. 7) were carried out (ORIGIN 8 Version 8E) [9].

Particle size and zeta potential

The average particle size of prepared 5-FU QDs was measured by particle size analyzer (NANOPHOX-NX0088). 5-FU QDs were diluted with distilled water to make 5% v/v. The particle size distributions were estimated by setting the intensity of the scattered light at a wavelength of 750 nm and the scattering angle (θ) of 90 °. The particle size of Eudragit E PO coated QDs was determined as depicted in (fig. 8). Zeta potential of Eudragit E PO coated QDs was determined by Beckman Coulter as shown in (fig. 9), to analyze particle size and zeta potential samples were diluted with ultra pure water.

Percentage yield, drug loading and drug content

The QDs and the drug were taken 1:2 w/w. Further, the yield of this batch was determined. Then, 1 mg of sample was taken from obtained yield and added in 10 ml of methanol. Further, dilutions were prepared, and absorbance was taken, it resulted that the absorbance value obeys the beer's and lambert's law. Samples were measured at an absorbance of 266 nm in double beam UV Spectrophotometer. Final calculations were done, and percentage yield, drug loading and drug content were determined.

Percentage yield (%)

$$\frac{\text{weight of drug loaded QDs}}{\text{Weight of drug loaded QDs} + \text{Initial weight of polymer}} \text{X } 100$$

The percentage yield of Eudragit E PO coated QDs was determined by using above formula. The values obtained were put into the above formula and percentage yield was determined.

Drug loading (%)

$$\frac{\text{Actual drug content in sample of particles}}{\text{Weight of drug loaded QDs}} \text{ X } 100$$

The drug loading of prepared Eudragit E PO loaded QDs was determined by using above formula. The obtained values were put into a formula, and drug loading was calculated.

Drug content (%)

The QDs and Drug were taken in 1:2 ratios. Further, yield was determined. Then, 1 mg of QDs were taken from obtained yield and diluted in 10 ml of methanol. Further, dilutions were prepared, and absorbance was taken, it resulted that the absorbance value obeys the Beer's and Lambert's law. Final calculations were done, and drug content was determined.

Scanning electron microscopy (SEM)

Scanning electron microscopy (SEM) was used to verify the uniformity of particle shape and size. SEM of 5-FU QDs was carried out in the solid state. The surface morphology of the samples was observed under a scanning electron microscope (Beckman Coulter, NNSEM 450) as shown in (fig. 10). The samples were mounted on aluminium stab by using a double-sided adhesive tape. Then it was placed in an ion coater unit (Model: IB-2, Hitachi, Tokyo, Japan) for gold coating (200 A). During gold coating process the samples were exposed to a vacuum of 10-50 mm. After this, an accelerating voltage of 15 kV and 10 kV was applied, and the image was photographed by Asia Pentax Camera. SEM images of drug loaded QDs and Eudragit E PO coated QDs were determined [9].

Fourier transforms infrared spectroscopy (FT-IR)

The FT-IR of pure 5-FU was carried out to determine the functional groups present in it as depicted in (fig. 11) [8, 10]. The FT-IR of Eudragit E PO was also performed as shown in (fig. 12). The FT-IR of zinc chloride and Eudragit E PO was carried out to determine the interaction between drug and excipients as shown in (fig. 13). The FT-IR of drug loaded QDs were done and interpreted. The FT-IR of Eudragit E PO coated QDs was done and interpreted. The overlay of drug loaded QDs and Eudragit E PO coated QDs is shown in (fig. 14).

***In vitro* drug release study**

First, the phosphate buffer of pH 4.0 was prepared by dissolving 5.04 g of disodium hydrogen phosphate and 3.019 g of potassium dihydrogen phosphate in distilled water (1000 ml) and final pH was adjusted by addition of glacial acetic acid [11]. *In vitro* drug release was performed by putting 20 mg of Eudragit E PO coated QDs in 900 ml phosphate buffer (pH-4.0) using USP type II (Paddle) dissolution apparatus (TDT 08L Basic Electrolab) under stirring at 100 RPM. The temperature of dissolution medium was maintained at 37±0.5 °C. Samples were withdrawn periodically at 0 min, 5 min, 10 min up to 95 min and the volume was replaced immediately with fresh medium. Sample solutions were filtered and analyzed by measuring absorbance in at 266 nm. Further, (%) drug release was calculated as depicted in (fig. 15).

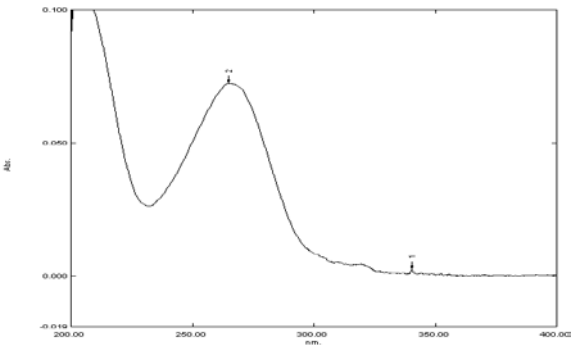

Fig. 1: Spectra of 5-FU

RESULTS AND DISCUSSION

5-FU was estimated by using UV spectrophotometer**.** The solvent, methanol was selected on the basis of solubility of 5-FU in it compared to other solvents chloroform and distilled water tested earlier in preliminary studies. Therefore, in the analytical method development, methanol was used as a solvent. Initially, λ max of 5-FU in methanol was determined. It was found at 266 nm. So further, the estimation of 5-FU was carried out at 266 nm by using UV spectrophotometer. The dilutions of definite concentrations were prepared. Samples were diluted if necessary. The absorbance of samples was noted. It was found that the concentration ranges 5 to 25 µg/ml obey Beer's and Lambert's law. For the stated range of dilutions for calibration curve, absorbance was found in proportion with the concentrations giving the value of $R^2$0.995.

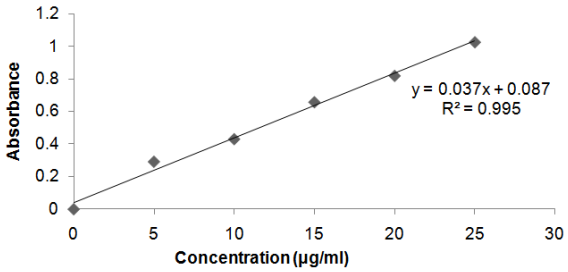

Fig. 2: Calibration curve of 5-FU

Table 4: Batches of uncoated QDs

Batch	(%) Yield obtained
B_1	12.00±0.15
B_2	61.25±0.21
B_3	0.053±0.06
B_4	0.057±0.09
B_5	0.049±0.04

Sample size n=03, Values are expressed as mean±SD

Preparation of uncoated QDs

The yield of uncoated QDs was found the least (0.049 %±0.04) for batch B_5 and the highest (61.25 %±0.21) for batch B_2. Therefore, the batch B_2, with maximum yield, was treated for further experimentation.

As quantum dots consist of semiconductor metal, it was wise to use zinc as a semiconductor as the core-forming metal of the quantum dots due to its non-toxic nature, easy availability in the laboratory and in addition, it possesses antimicrobial action [7]. Zinc is also present as a trace element in a human body. Zinc is II-VI group element in periodic table having the property of fluorescence upon the incidence of ultraviolet rays. Therefore, this property of zinc can

be utilized for imaging of anticancer drug delivered at the site through its suitable drug delivery form. In the preparation of QDs, the temperature of reaction mixture was kept not more than 60 °C since it was found an important process variable. The addition of concentrated nitric acid to zinc chloride showed reddish colour and further addition of methanol downs to faint. The resultant QDs were discrete and free flowing. After preparation of batches of uncoated QDs, were evaluated for percentage yield. The batch having most percentage yield was selected for drug coating as depicted in (table 4).

Till date some researchers have focused on cadmium–selenium QDs for targeting delivery of drug and some have worked on zinc-magnesium QDs for tumor targeting. Here, in this work very simple method of preparation was used to prepare zinc oxide quantum dots, which is feasible in the laboratory. In this work, it was an attempt to prepare ready to formulate QDs in the liquid dosage form to administer parenterally. Therefore, QDs were further coated by pH sensitive polymer to obtain the drug release at desired site, which was rarely mentioned in the earlier literature.

Table 5: Batches of drug loaded QDs

Batch	QD: drug	Solvent and volume of solvent used	Coating solvent
B_1	1: 0.5	Methanol-5 ml	Cold water-5 ml
B_2	1:1	Methanol-5 ml	Cold water-5 ml
B_3	1:1	Methanol-5 ml	Petroleum ether-5 ml
B_4	1:1	Methanol-5 ml	Acetone-5 ml
B_5	1:2	Methanol-5 ml	Cold water-5 ml

Table 6: Batches of Eudragit E PO coated QDs

Batch	Time is taken for release (min)	drug release (%)
B_1	95	56±0.001
B_2	95	68±0.007
B_3	95	80±0.014
B_4	95	99±0.011

Sample size, n=03, Drug release is expressed as mean±SD

Preparation of drug loaded QDs

Few batches are having different QDs: Drug ratios were prepared and evaluated for their drug loading, drug content and drug release as depicted in (table 5). Among the batches B_1 to B_5, the ratio 1:1 (QDs: Drug) was found the best. The batch, with higher drug loading, drug content and drug release was selected. Though the solvents used to load the drug were used in the same quantity that is 5 ml, the drug loading was found better by using cold water compared to petroleum ether and acetone.

Preparation of Eudragit E PO coated QDs

Eudragit E 100 and Eudragit E PO were the polymers selected for coating over the drug loaded QDs. Due to unsatisfactory results of coating efficiency of Eudragit E 100, finally, Eudragit E PO was selected for coating. The purpose of Edragit coating was to make QDs more convenient for drug delivery by improving physical properties. Further, it was decided to incorporate drug loaded QDs in chloroform due to the solubility of Eudragit E PO in chloroform and due to evaporation of chloroform it was possible to coat drug loaded QDs by Eudragit E PO. Chloroform was the solvent kept common for all the batches as the drug was insoluble in it.

The QDs at this stage were white in colour and needed more time to dry. The ratios of drug loaded QDs and Eudragit E PO concentration were varied. The batch, which showed maximum drug release was considered the best (table 6).

Differential scanning calorimetry (DSC)

DSC is considered as a tool to investigate the melting behaviour of crystalline materials. DSC of 5-fluorouracil and Eudragit E PO coated QDs were performed. The DSC curve of 5-FU exhibited the corresponding peak at 286 °C corresponding to its melting point. Eudragit E PO coated QDs exhibited a peak at temperature 272 °C. This shifting of the endotherm suggested a possible interaction of 5-FU and Eudragit E PO coated QDs. This justifies that polymer has been loaded upon the drug loaded QDs. To achieve stability, compatibility between the drug and the polymer must be ensured which can be confirmed by the DSC and further by XRD studies.

X-ray diffraction studies (XRD)

An XRD peak mainly depends on the crystal size as they indicate the crystalline nature at a particular value at 2θ range. In this study, pure 5-fluorouracil has shown a sharp peak indicating its multi-crystalline nature. Eudragit E PO diffractograms showed peaks indicating its amorphous nature. The diffractogram of Eudragit E PO coated QDs also showed the crystalline nature. The diffractogram of Eudragit E PO was found different from the Eudragit E PO coated QDs, as it was noticed that amorphous nature of polymer was changed into crystalline nature in Eudragit E PO coated QDs.

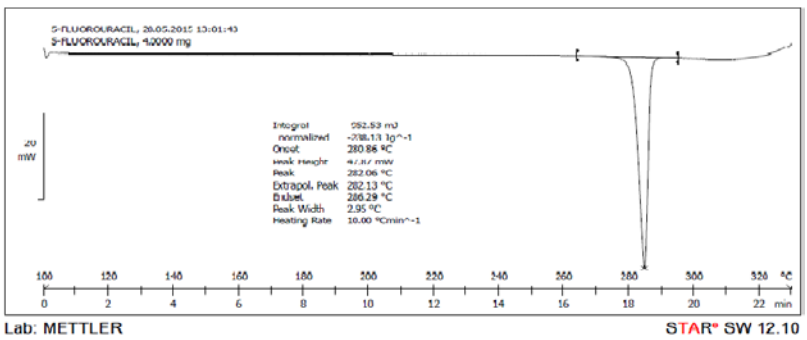

Fig. 3: DSC graph of 5-FU

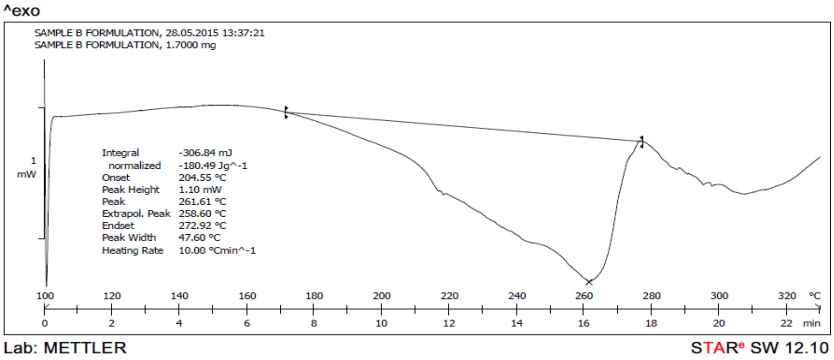

Fig. 4: DSC graph of Eudragit E PO coated QDs

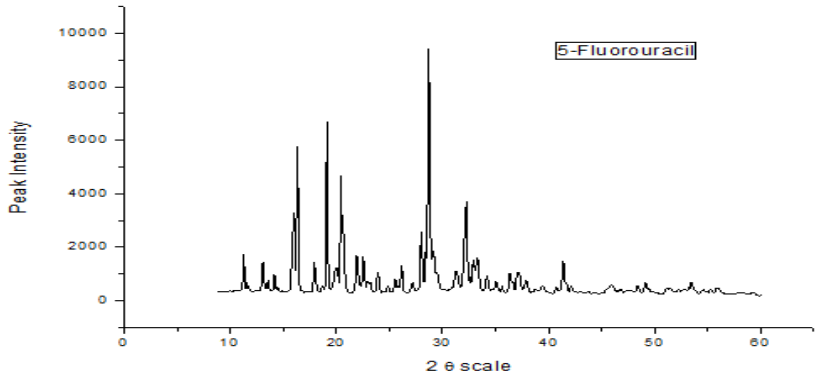

Fig. 5: XRD of 5-FU

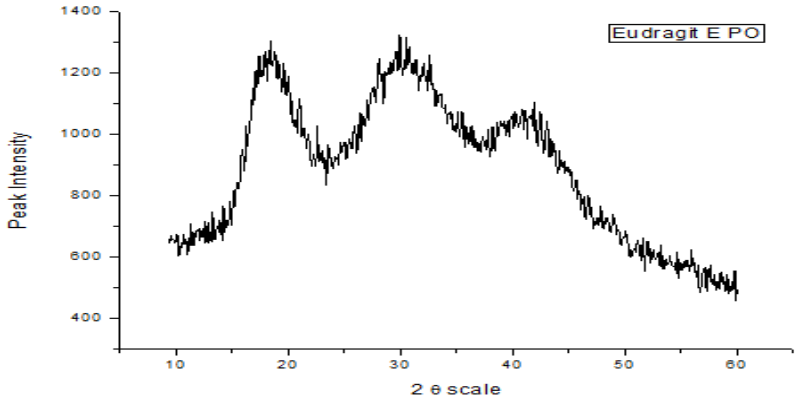

Fig. 6: XRD of Eudragit E PO

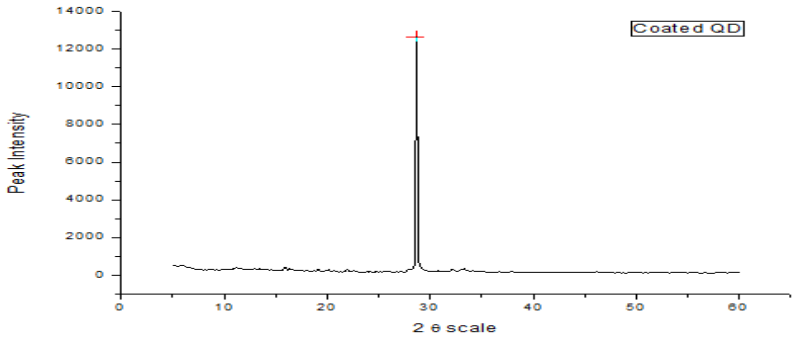

Fig. 7: XRD of Eudragit E PO coated QDs

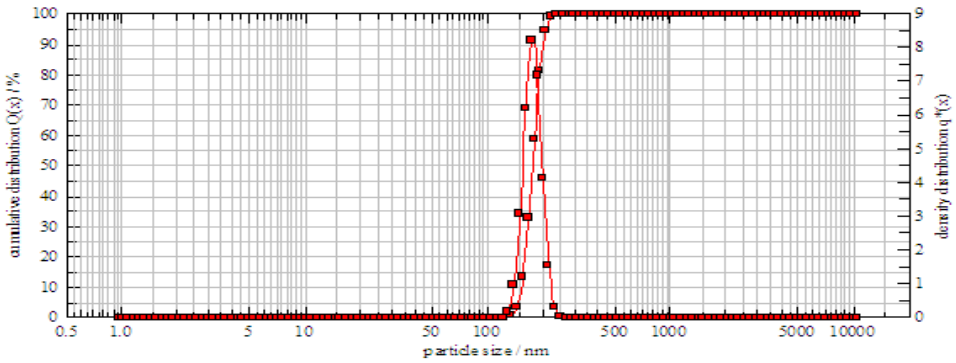

Fig. 8: Particle size results of Eudragit E PO coated QDs

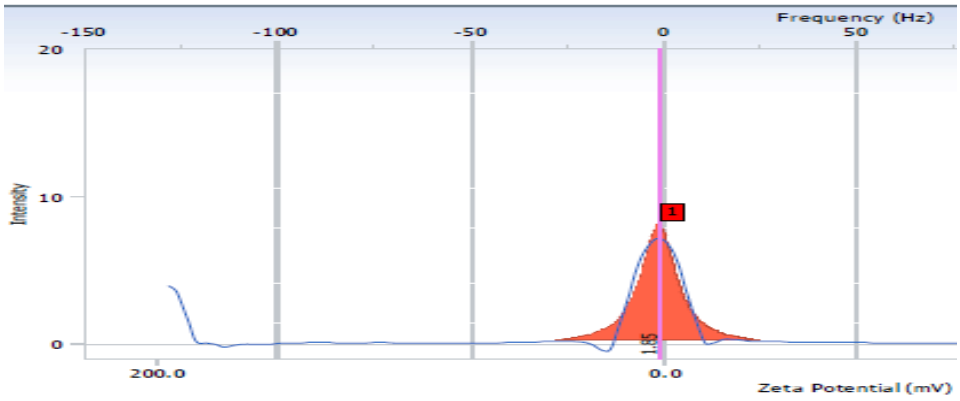

Fig. 9: Zeta potential results of Eudragit E PO coated QDs

Particle size and zeta potential

The particle size of the formulation of 5-FU QDs (Batch B_5) showed in the range of 151.01 nm to 222.91 nm. The mean particle size of the optimized formulation batch was 201.92 nm. It is visually observed that the particle size was found to be increased after coating of Eudragit E PO. The increase in particle size is in agreement with the QDs reported by Denim IT, Kadioglu D [7]. The polydispersity index was found 0.181. The prepared QDs were more uniform in particle size. Wider the particle size, the greater is the polydispersity index. This was determined three times (n =3) in order to ensure reproducibility to minimize the error. Zeta potential of the optimized batch was found at+1.85 mV and it further proves the stability of the prepared Eudragit E PO coated QDs, which justifies the rationale of preparing stable QDs, as stable QDs can be easily dispersed. Tummala S *et al.* have reported preparation and evaluation of enteric coated nanoparticles by extrusion spheronization technique for colorectal delivery [9]. However, in the present work, it was an attempt to prepare enteric coated QDs.

Table 7: Results of Percentage yield, Drug loading and Drug content

Batch No.	Yield (%)	Drug loading (%)	Drug content (%)
B_5	74±0.001	85.58±0.08	95±0.015

Sample size, n=03; Values are expressed as mean±SD

Percentage yield, drug loading and drug content

Based on the evaluation parameters of drug content, drug loading and percentage yield, 5-FU QDs of ratio 1:2 were optimized. The drug content of the same batch was found maximum compared to other batches. Definite numbers of batches were prepared, and each batch was evaluated for drug loading. The batch is having ratio 1:2 of QDs: the drug was selected as this batch had maximum drug loading. The same batch had most of the percentage yield. So, as a result, these parameters were taken into consideration while selecting the best batch as shown in (table 7). The percentage yield, the drug content and drug loading were found less in batches B_1 to B_4 compared to B_5.

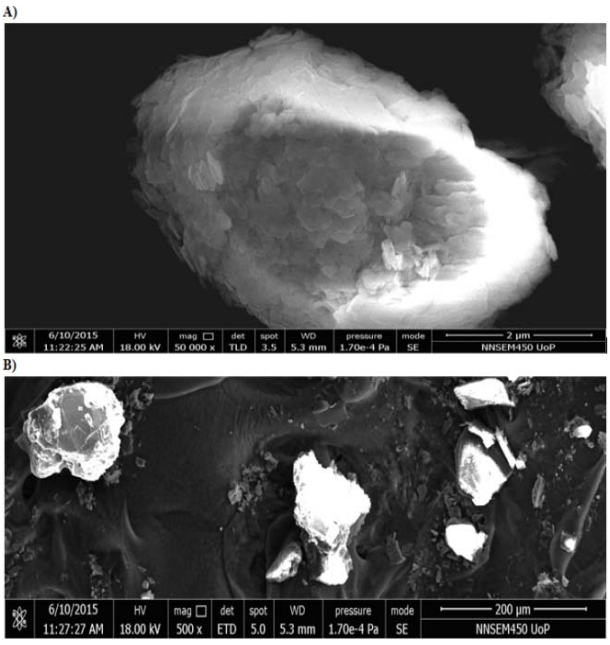

Fig. 10: SEM of A) drug loaded QDs; B) Eudragit E PO coated QDs

Scanning electron microscopy (SEM)

The surface morphology and shape of the 5-FU QDs were analyzed by scanning electron microscopy for optimized formulation confirms that 5-FU QDs are oval in shape with a smooth surface. Scanning electron microscopy was performed for drug loaded QDs and Eudragit E PO QDs of ratio 1:2 to obtain more information on the particle size and morphology. The photos of drug loaded QDs had shown that they have different morphologies as compared to formulated Eudragit E PO QDs. Moreover, the drug loaded QDs were observed with a rough surface, whereas Eudragit E PO coated QDs had a smooth surface.

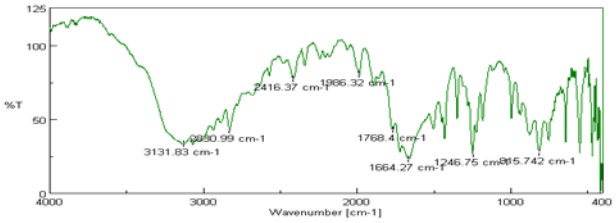

Fig. 11: FT-IR of 5-FU

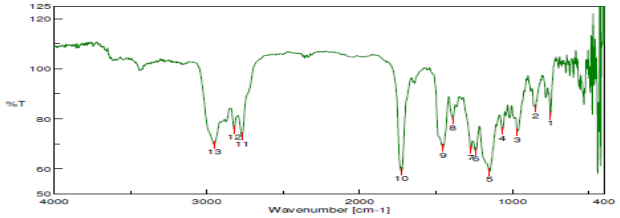

Fig. 12: FT-IR of Eudragit E PO

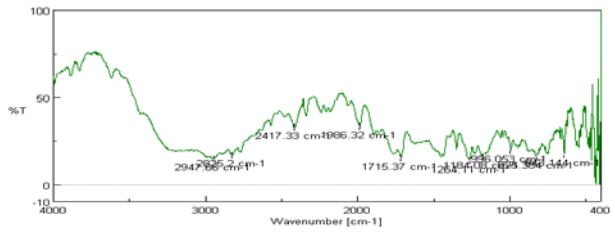

Fig. 13: FT-IR of drug-polymer mixture

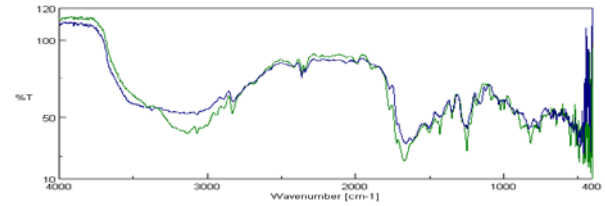

Fig. 14: FT-IR of overlay of drug loaded QDs and Eudragit E PO coated QDs

Fourier transform infrared spectroscopy (FT-IR)

DSC is not the only studying tool to demonstrate an effective drug-excipient interaction, but a non-thermal tool, FTIR can also be used. FTIR was performed to study the possible interactions between 5-FU and other excipients. The FTIR spectrum of drug loaded QDs was also performed. The spectrum shows the typical characteristics of drug loaded QDs (e. g., the OH-stretching at 3067 cm−1, the methylene bands C–H at 2830 and 2360 cm-1, the C=O stretching vibrations due to carboxylic groups at 1985 cm−1, the 1671 cm−1 band due to C-C bonds conjugated with C-O and COO− groups). FTIR spectra of Eudragit E PO reveals the characteristic absorption bands observed at: 3377.71 cm^{-1}, the weak band of O-H stretching; 3070 cm^{-1}, strong band of aromatic C-H stretching; 2827 cm^{-1}, the strong band of alkene C-H stretching; 1506.13 cm^{-1}, the intermediate to strong band of C=C stretching of the alkene; 1348.96 cm^{-1}, the strong band of C-O stretching of the phenolic group; 1156 cm^{-1}, the strong band of C-C stretching. The FTIR spectrum of pure drug 5-FU is officially matched with the FTIR spectrum of polymer and drug loaded QDs. As all major peaks for the drug in the QDs mixture are observed, it has been concluded that there is no any kind of incompatibility between drug, polymer and metal [10].

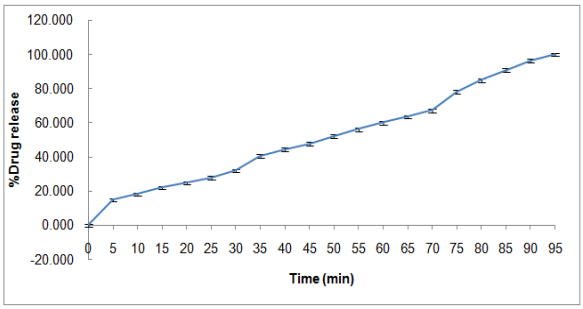

Fig. 15: Drug release of Eudragit E PO coated QDs Sample size, n=03, Values are expressed as mean±SD

Table 8: Drug release study

Time (min)	% Drug release
0	0.000
5	14.969±0.05
10	18.258±0.09
15	22.022±0.012
20	24.890±0.017
25	27.774±0.018
30	32.046±0.041
35	40.463±0.022
40	44.346±0.015
45	47.792±0.011
50	52.172±0.08
55	56.116±0.001
60	60.081±0.014
65	63.608±0.018
70	67.153±0.021
75	78.042±0.030
80	84.869±0.06
85	90.815±0.04
90	96.334±0.017
95	100.01±0.05

Sample size, n=03; Values are expressed as mean±SD

Table 9: linear regression analysis of Eudragit E PO coated QDs

Batch	Best fit model	R-value	K value
B_1	Zero order	0.9902	1.0501
B_2	Matrix	0.9335	8.3558
B_3	Peppas	0.9753	3.5119
B_4	Hixon Crowell	0.8209	-0.0065

***In vitro* drug release study**

The percentage drug release from Eudragit E PO coated QDs was observed by using USP dissolution apparatus II in phosphate buffer at pH 4.0. The percentage drug release of optimized batch B_5 having 1:2 QDs-drug ratios was found maximum at time 95 min is given in

(table 8). The best fit model was found to be zero order as depicted in (table 9). The effective concentration of the drug must be reached to the site with a carrier to exert the action of the drug. As the cancerous target tissues or cells have an acidic environment, Eudragit E PO is expected to get released in the pH range of 1-5 due to its solubility at this acidic pH range. Intravenous route of administration for QDs is suitable because the drug is not expected to release at blood pH 7.4 but at acidic pH (pH 1-5) of cancerous cells.

CONCLUSION

It was possible to prepare successfully Eudragit E PO coated QDs for delivery of 5-FU. It was found that the optimized batch of QDs has potential so that it can be utilized in future for imaging of cancer cells and targeting delivery of 5-FU.

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CONFLICT OF INTERESTS

All authors declare that they have no conflict of interest.

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